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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/643,623 | 08/19/2003 | Janos Szamosi | AM100224 P1 | 4463 |

25291 7590 05/16/2008

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| EXAMINER | |
|---|---|
| SHEIKH, HUMERA N | |
| ART UNIT | PAPER NUMBER |
| 1618 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 05/16/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/643,623 | SZAMOSI ET AL. | |
| | Examiner | Art Unit | |
| | Humera N. Sheikh | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,5,8-10,12 and 15-37* is/are pending in the application.

4a) Of the above claim(s) *15-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 8-10, 12 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### Status of the Application

Receipt of the Request for Continued Examination under 37 C.F.R. 1.114, the Amendment and Applicant's Arguments/Remarks, all filed 04/01/08 is acknowledged.

Applicant has overcome the following rejection(s) by virtue of the amendment and/or persuasive remarks: (1) The 35 U.S.C. 112, 1st paragraph rejection of claim 1 has been withdrawn; (2) The 35 U.S.C. §102(b) rejection of claims 1-4, 5, 7-9 and 14 over Mizumoto *et al.* (US 5,576,014) has been withdrawn; and (3) The 35 U.S.C. §102(e) rejection of claims 1, 4, 5, 7-9 and 14 over Shimizu *et al.* (U.S. Patent No. 6,299,904) has been withdrawn.

Claims 1, 5, 8-10, 12 and 15-37 are pending in this action. Claims 1, 5 and 9 have been amended. New claims 32-37 have been added. Claims 15-31 have previously been withdrawn (based on non-elected invention). Claims 1, 5, 8-10, 12 and 32-37 are rejected.

* * * * *

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01 April 2008 has been entered.

* * * * *

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1, 5, 8-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wehling *et al.* (U.S. Pat. No. 5,178,878) in view of Mauger *et al.* (U.S. Pat. No. 5,728,403).**

**Wehling *et al.* ('878)** teach an effervescent dosage form in the form of a rapidly disintegrating tablet, whereby the tablet comprises a pharmaceutical active ingredient (col. 3, lines 45-58); (col. 4, lines 56-62); lubricants such as polyethylene glycol, hydrogenated and partially hydrogenated vegetable oils, animal fats, polyoxyethylene monostearate, light mineral oils and the like in amounts of up to 1.5 wt.% (col. 9, lines 8-20); and water soluble excipients

such as saccharides, sugars, invert sugars and the like in amounts of up to 60 wt. % (col. 7, lines 35-51 and Example I). Sweeteners can be added in amounts of up to about 20 wt. %. Suitable sweeteners include aspartame (Table II – col. 13). Suitable excipients disclosed include mannitol (Tables I & II). Additional polymers include waxes (col. 11, line 50). The tablet has a hardness of about 1.5 kilo pounds (col. 10 lines 30-42).

Additional adjuvants disclosed include flavors, diluents, colors, binders, fillers, compaction vehicles and non-effervescent disintegrants (col. 7, lines 29-34).

Wehling *et al.* do not teach the selective hydrogenated oils such as palm kern oil or hydrogenated cottonseed oil.

**Mauger *et al.* ('403)** teach a pharmaceutical composition for oral administration comprising mixtures of monoglycerides, diglycercides and triglycerides derived from vegetable oils such as palm kernel oil and cottonseed oils. Specific mixtures taught include Cotomar®, Wecobee FS®, Witepsol E7S® and Massa Estariorm A®, which consists of a mixture of triglycerides, diglycerides and monoglycerides of saturated fatty acids. The (tri)glycerides aid in masking the taste of orally administered drugs (col.1, lines 56-60) and also cause the composition to melt at body temperature (see col. 2, lines 39-63).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the specific vegetable oils such as cottonseed and palm kern oils as taught by Mauger *et al.* within the tablet compositions of Wehling *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Mauger *et al.* teach a pharmaceutical composition that comprises mixtures of monoglycerides, diglycercides

and triglycerides derived from vegetable oils such as palm kernel oil and cottonseed oils and teach that the glycerides aid in masking taste of drugs and enable the composition to melt at body temperature. The expected result would be an improved, highly effective and palatable tablet for drug delivery.

* * * * *

**Claims 1, 5, 8-10, 12 and 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizumoto *et al.* (U.S. Pat. No. 5,576,014) in view of Mauger *et al.* (U.S. Pat. No. 5,728,403).**

**Mizumoto *et al.* ('014)** teach an intrabuccally dissolving compressed moldings in the form of a tablet that show quick disintegration and dissolution and having an adequate hardness of preferably 1.0 kg or more (see Abstract); (col. 4, lines 35-62); (col. 11, lines 23-40).

The tablets comprise suitable saccharides that include lactose, mannitol, glucose, sucrose, xylitol, maltose, sorbitol and the like. These saccharides may be used alone or as a mixture of two or more (col. 6, lines 37-46) and (Examples). The saccharides may be added in amounts of from 2 to 20% by weight (col. 14, line 6). The tablets also comprise any suitable active ingredient (col. 7, line 50 – col. 10, line 2).

Lubricants are included in the composition and include sucrose fatty acid esters, polyethylene glycol, talc, stearic acid and the like. These may be used alone or as a mixture of two or more (col. 13, lines 50-65).

Additive agents can be added and include disintegrating agents, binding agents, souring agents, artificial sweeteners such as aspartame, perfumes, lubricants, coloring agents and the like (col. 13, lines 32-49).

While Mizumoto *et al.* do not teach all the instantly claimed amounts and/or ranges, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). It is the position of the Examiner that Applicants have not demonstrated any unexpected or surprising results attributable to the claimed amounts. The prior art teaches a similar tablet formulation as claimed that is comprised of similar components used for the same field of endeavor as that of the Applicant's invention.

Mizumoto *et al.* do not teach the selective hydrogenated oils such as palm kern oil or hydrogenated cottonseed oil.

**Mauger *et al.* ('403)** teach a pharmaceutical composition for oral administration comprising mixtures of monoglycerides, diglyercides and triglycerides derived from vegetable oils such as palm kernel oil and cottonseed oils. Specific mixtures taught include Cotomar®, Wecobee FS®, Witepsol E7S® and Massa Estariorm A®, which consists of a mixture of triglycerides, diglycerides and monoglycerides of saturated fatty acids. The (tri)glycerides aid in masking the taste of orally administered drugs (col.1, lines 56-60) and also cause the composition to melt at body temperature (see col. 2, lines 39-63).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the specific vegetable oils such as cottonseed and palm kern oils as taught by Mauger *et al.* within the tablet compositions of Mizumoto *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Mauger *et al.* teach a pharmaceutical composition that comprises mixtures of monoglycerides, diglycercides and triglycerides derived from vegetable oils such as palm kernel oil and cottonseed oils and teach that the glycerides aid in masking taste of drugs and enable the composition to melt at body temperature. The expected result would be an effective drug delivery tablet.

* * * * *

**Claims 1, 5, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Makino *et al.* (U.S. Pat. No. 5,501,861).**

**Makino *et al.* ('861)** teach a fast dissolving tablet comprising a pharmacologically active ingredient; carbohydrate including starch sugars, sugar alcohols, tetroses and so on, in amounts of 10 to 90% by weight; and lubricants that include sucrose fatty acid esters, polyethylene glycol, talc and stearic acid (see columns 1, lines 9-15); (col. 3, lines 21-24); (col. 6, lines 1-7). The tablets have a hardness of 3 to 20 kg (Claim 1).

Suitable carbohydrates and sugars taught include sucrose, lactose, glucose and maltose. Sugar alcohols disclosed include sorbitol, mannitol, reduced malt syrup (maltitol), reduced starch saccharides, xylitol and the like (col. 5, lines 1-24) and Examples.

Additives taught include disintegrators, binders, acids, foaming agents, artificial sweeteners such as aspartame, flavorants, lubricants, colorants, etc. (col. 5, lines 55-67).

While Makino *et al.* do not teach all the instantly claimed amounts and/or ranges, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). It is the position of the Examiner that Applicants have not demonstrated any unexpected or surprising results attributable to the claimed amounts. The prior art teaches a similar tablet formulation as claimed that is comprised of similar components used for the same field of endeavor as that of the Applicant's invention.

Given the explicit teachings of Makino *et al.*, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

**Claims 1, 8-9, 14, 32 and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu *et al.* (U.S. Patent No. 6,299,904).**

**Shimizu *et al.* ('904)** teach a solid preparation, which is a tablet, having fast disintegration that comprises (i) a pharmaceutically active ingredient; (ii) one or more water-soluble sugar alcohols selected from the group consisting of sorbitol, maltitol, reduced starch

saccharide, xylitol, reduced palatinose and erythritol and (iii) low-substituted hydroxypropycellulose (see Abstract); (col. 1, lines 8-57); (Claims 1 & 6). Two or more water-soluble sugar alcohols can be used as a mixture in a given ratio (col. 4, line 66 – col. 5, line 2).

Lubricants are disclosed in the composition and include: sucrose fatty acid ester, polyethylene glycol, talc, stearic acid, etc. Polyethylene glycol can be used in an amount of 0.01 to 10 weight parts (col. 6, lines 26-34).

Additives are disclosed in the composition and include: artificial sweeteners such as aspartame, flavorants, lubricants, colorants, stabilizers, disintegrators, etc. (col. 5, line 59 – col. 6, line 25).

The tablets have a hardness of about 2 to about 20 kg (col. 8, lines 5-8). Applicant's recite a hardness of "less than about 2 kp", which nonetheless, would read on the "about 2 kp" taught by Shimizu.

***Response to Arguments***

Applicant's arguments filed 04/01/08 have been fully considered and were found to be partially persuasive.

- **35 U.S.C. §112, 1st paragraph rejection:**

Applicant argued, "The phrase to which the Examiner objected has been removed by the present amendment."

This argument has been considered and was found persuasive. Accordingly, the 35 U.S.C. 112, 1st paragraph rejection has been withdrawn.

- **35 U.S.C. §102 rejection over Mizumoto et al. ('014):**

Applicant argued, "Nowhere does Mizumoto disclose or suggest a fast dissolving granulation and/or the combination of a saccharide and low melting point compound to form a fast dissolving granulation wherein the fast dissolving granulation comprises about 30% to about 75% of the weight of the tablet as currently amended independent claim 1 sets forth. "

This argument was persuasive by virtue of the amendment reciting the percentage of about 30% to about 75% of the weight of the tablet. Accordingly, this rejection has been withdrawn.

- **35 U.S.C. §102 rejection over Shimuzu et al. ('904):**

Applicant argued, "Nowhere does Shimizu disclose or suggest a fast dissolving granulation and/or the combination of a saccharide and low melting point compound to form a fast dissolving granulation wherein the fast dissolving granulation comprises about 30% to about 75% of the weight of the tablet as currently amended independent claim 1 sets forth. "

This argument was persuasive by virtue of the amendment reciting the percentage of about 30% to about 75% of the weight of the tablet. Accordingly, this rejection has been withdrawn.

- **35 U.S.C. §103(a) rejection over Wehling et al. ('878) in view of Mauger et al. ('403):**

Applicant argued, "Wehling is directed to a pharmaceutical dosage form that comprises microparticles combined in a tablet with an effervescent disintegration agent (see abstract). Wehling's list of optional lubricants includes high melting point solids such as sodium benzoate."

Applicant's arguments were not persuasive. It is agreed that Wehling teaches an effervescent disintegration agent. However, the instant claims utilize "comprising" claim language and thus permit the additional agents of Wehling, including the effervescent agents as well as the optional high melting point solids. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004).

With regards to the instant amounts of the fast dissolving granulation (about 30% to about 75% of the tablet weight), the Examiner points out that differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Applicant's arguments that Mauger is directed to taste masking coating and not a tablet was not persuasive. It is agreed that Mauger teaches a coating. However, Mauger was relied upon to demonstrate the teaching that it is known to incorporate mixtures of mono-, di- and

triglycerides, whereby the glycerides provide for aiding in taste-masking of drugs and enables a composition to melt at body temperature. The secondary reference thus teaches that mixtures of mono-, di- and triglycerides are well known and routinely used in the art. The Mauger reference further teaches the use of the selective hydrogenated oils, such as palm kernel oil and hydrogenated cottonseed oil. Thus, this rejection has been maintained.

- **35 U.S.C. §103(a) rejection over Mizumoto et al. ('014) in view of Mauger et al. ('403):**

Applicant argued, ""In contrast to Applicant's invention, Mizumoto neither teaches that a saccharide is required (Mizumoto requires at least two saccharides with specified moldabilities) or that a water soluble excipient in combination with a low melting point solid forms a fast dissolving granulation."

This argument was not persuasive since the instant "comprising" claim language permits the presence of additional components, asides from those recited, including the use of more than one saccharide disclosed by Mizumoto. Mizumoto also discloses sucrose fatty acid esters, polyethylene glycol, stearic acid and the like, which would read on the low melting point compounds claimed by Applicant. Furthermore, the "consisting essentially of" language would not exclude more than one saccharide, as saccarides are a permissible component of the instant invention.

Applicant argued, "The deficiencies of Mizumoto are not cured by Mauger. Mauger is directed to a taste masking coating not to a tablet that dissolves readily. Arguably Mauger does not even teach a fast dissolve coating much less a fast dissolving tablet."

These arguments were not persuasive. Mauger was relied upon to demonstrate the teaching that it is known to incorporate mixtures of mono-, di- and triglycerides, whereby the glycerides provide for aiding in taste-masking of drugs and enables a composition to melt at body temperature. The secondary reference thus teaches that mixtures of mono-, di- and triglycerides are well known and routinely used in the art. The Mauger reference further teaches the use of the selective hydrogenated oils, such as palm kernel oil and hydrogenated cottonseed oil. Thus, Mauger amply remedies the deficiency of Mizumoto.

- **35 U.S.C. §103(a) rejection over Makino ('861):**

Applicant argued, "Applicants claim a tablet of a hardness of less than about 2 kp. Makino claims a tablet having a hardness of '3 to 20 kp'. The instant fast dissolve tablet yields a tablet with substantially different physical properties of Makino's tablet."

This argument was not persuasive. Applicant argues the properties obtained from based on the hardness levels taught and the hardness levels claimed. This argument was not persuasive since Makino is also directed to a fast dissolving tablet. The tablet can include low melting point compounds. Moreover, the prior art clearly teaches fast dissolving tablets, that can comprise low melting point compounds (i.e., polyethylene glycol) as well as water-soluble excipients (i.e., saccharides). The property argued by Applicant (fast dissolving) is insufficient to establish patentability of the claims as presently recited.

The rejection has been maintained.

***Conclusion***

--No claims are allowed at this time.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1618

*hns*

May 12, 2008